SYNLETT
Spotlight 60

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Pyrrolidine-2-carboxylic Acid (L-Proline)

Compiled by Abhimanyu S. Paraskar

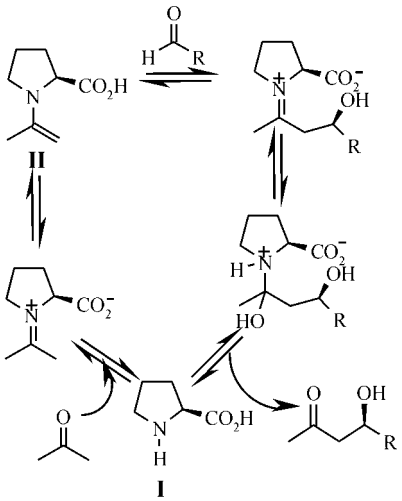
Abhimanyu S. Paraskar obtained his Masters degree in chemistry from Amravati University, Maharastra, India. He is currently working on his PhD thesis under the supervision of Dr. Arumugum Sudalai at National Chemical Laboratory, Pune, India.

National Chemical Laboratory, Process Development Division, Pashan Road, Pune-411008, India
E-mail: asparaskar@pd.ncl.res.in

Introduction

Pyrrolidine-2-carboxylic acid commonly known as L-Proline (**I**) has shown, in recent times, excellent catalytic activity, in catalyzing a wide variety of reactions such as aldol,[1,2] Mannich,[3–5,10–12] Michael,[6–9] in a highly enantioselective manner. These reactions have produced a variety of useful chiral materials for organic synthesis.

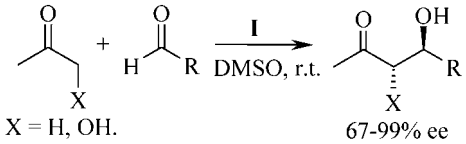
Most of the L-Proline (I) catalyzed reactions are believed to involve enamine (**II**) as key intermediate in its catalytic cycle (Scheme 1).



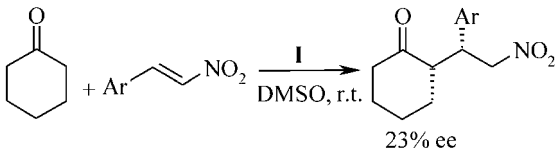
Scheme 1 Proline – catalytic cycle for aldol reaction.

Abstracts

L-Proline (**I**) catalyzes the asymmetric aldol reaction between acetone and various aldehydes. In the case of hydroxy acetone, it gives *anti*-diols in excellent diastereo- and enantioselectivities.[1,2]



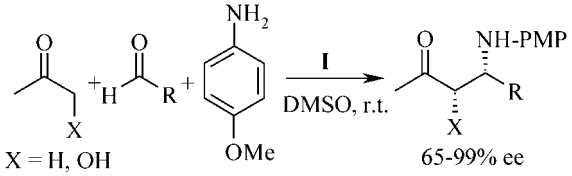
L-Proline catalyzes the Michael reaction of ketones with nitro olefins to provide a variety of chiral Michael addition products.[6–9]



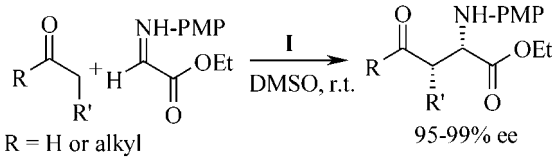
Synlett 2003, No. 4, Print: 12 03 2003.
Art Id.1437-2096,E;2003,0,04,0582,0583,ftx,en;V06103ST.pdf.

ISSN 0936-5214

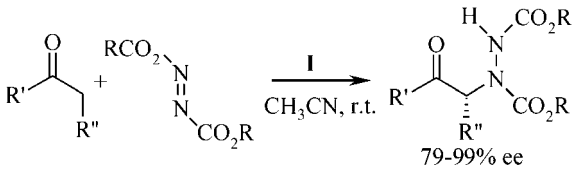
L-Proline catalyzes asymmetric the three component coupling involving Mannich reaction of acetone aldehydes and aryl amines to give β-amino ketones. In case of hydoxyacetone it gives α-hydroxy β-amino ketones in good to excellent ee. This reaction complements the Sharpless asymmetric aminohydroxylation.[3–5,10]



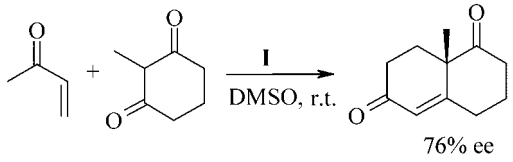
L-Proline catalyzes Mannich type reaction of protected α-imino ethyl glyoxylate with a variety of ketones to provide functionalized α-amino acids in high enantioselectivities.[11,12]



L-Proline catalyzes α-amination of ketones by applying azodicarboxylate as nitrogen source to give chiral α-hydrazino, α-amino ketones, and alcohols.[13]



Recently, **I** has proved to be the best catalyst for asymmetric Robinson annulation.[5]



References

(1) List, B.; Lerner, R. A.; Barbas III, C. F. *J. Am. Chem. Soc.* **2000**, *122*, 2395.
(2) Notz, W.; List, B. *J. Am. Chem. Soc.* **2000**, *122*, 7386.
(3) List, B. *J. Am. Chem. Soc.* **2000**, *122*, 9336.
(4) Sakthivel, K.; Notz, W.; Bui, T.; Barbas III, C. F. *J. Am. Chem. Soc.* **2001**, *123*, 5260.
(5) Groger, H.; Wilken, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 529.
(6) Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem.* **1996**, *61*, 3520.
(7) Hanessian, S.; Pham, V. *Org. Lett.* **2000**, *2*, 2975.
(8) List, B.; Pojarliev, P.; Martin, H. J. *Org. Lett.* **2001**, *3*, 2423.
(9) Bentancort, J. M.; Barbas III, C. F. *Org. Lett.* **2001**, *3*, 3737.
(10) List, B.; Pojarliev, P.; Biller, W. T.; Martin, H. J. *J. Am. Chem. Soc.* **2002**, *124*, 827.
(11) Cordova, A.; Notz, W.; Zhong, G.; Betancort, J. M.; Barbas III, C. F. *J. Am. Chem. Soc.* **2002**, *124*, 1842.
(12) Cordova, A.; Watanabe, S.; Tanaka, F.; Notz, W.; Barbas III, C. F. *J. Am. Chem. Soc.* **2002**, *124*, 1866.
(13) Kumaragurubaran, N.; Juhl, K.; Zhuang, W.; Bogevig, A.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 6254.